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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/035,918	12/28/2001	Rajiv Shah	047711-0293	2208

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EXAMINER	
PAK, YONG D	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 12/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/035,918	SHAH ET AL.	
	Examiner	Art Unit	
	Yong D Pak	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-8 and 10-43* is/are pending in the application.

4a) Of the above claim(s) *25-43* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-8 and 10-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The amendment filed on September 29, 2003, canceling claims 2 and 9 and amending claim 1, has been entered.

Claims 1, 3-8 and 10-43 are pending.

Election/Restrictions

Claims 25-43 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 8.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on June 27, 2003 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Response to Arguments

Applicant's arguments with respect to claim1, 3-8, and 10-24 have been considered but are moot in view of the new ground(s) of rejection.

Claim Rejections - 35 USC § 103

Claims 1, 3-5 are 19-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wohlfahrt et al. in view of Kenan et al.

Wohlfahrt et al. and art teach that glucose oxidases are susceptible to peroxide dependent inactivation (Wohlfahrt et al., pages 973-976, Greenfield et al., page 111 and Binyamin et al., abstract). Wohlfahrt et al. (form PTO-892) teach the active center of an *Aspergillus niger* glucose oxidase (pages 973-976). Wohlfahrt et al. teach that Met-561, is an amino acid involved in binding FAD to glucose oxidase. Met-561 is a target for peroxide because methionines are easily oxidized by peroxide and oxidation of the residues result in deactivation of the glucose oxidase.

It is well known in the art that teach that when a methionine is located at or near an active site, its oxidation to the sulfoxide is detrimental to the functioning of an enzyme (Koths et al. - U.S. Patent 4,752,585, Column 2, U.S. Patent 5,824,532, Column 2 and Estell et al., page 6518). Further, the presence of oxidized methionines causes structural changes in the protein and side effects such as aggregation of the protein.

The difference between the teaching of Wohlfahrt et al. and the instant invention is that the reference of Wohlfahrt et al. does not teach a method for generating a cDNA library and selectively screening for mutant galactose oxidases genes resistance against oxidation by peroxides and mutant galactose oxidase genes encoding active galactose oxidases .

However, cloning and screening methods for mutants generated by mutagenesis is extremely routine and well known. Any molecular textbooks or laboratory catalogs give ample teaching on generating a cDNA library by PCR or shuffling methods. Likewise, there are numerous techniques available in screening for the desired product,

by immunoassays, hybridization or by catalysis reactions (Kenan et al.). For example, one of ordinary skill in the art can screen for colonies resistant to a peroxidase by incubating the mutant genes in peroxide, similar to screening for colonies resistant to antibiotics. These methods of selecting for a mutant with a particular characteristics are well established in the art.

Since Wohlfahrt et al. and the art clearly teach the detrimental effects of oxidation of methionine in a protein, including a glucose oxidase, and teach methods of decreasing its susceptibility to oxidation by chemicals such as peroxides by generating mutants, and methods of generating mutants and screening for the desired products are also clearly taught in the art, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to generate mutant glucose oxidases, either randomly by PCR or by site-directed mutagenesis at oxidizable amino acids. It would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to screen colonies containing mutant glucose oxidases for a functional protein and one having resistance to oxidation by peroxide using the methods well known in the art. The motivation of making mutant glucose oxidases having reduced susceptibility to oxidation is to increase the stability and prolong its activity, especially its use in biosensors. Further, the motivation of screening colonies resistant to peroxide is to efficiently screen for the mutant enzymes instead of isolating and purifying enzymes. One of ordinary skill in the art would have had a reasonable expectation of success since site-directed and random mutagenesis is routinely

performed in the art and successful screening assays of colonies containing mutant proteins are well known and practiced in the art.

Claims 6-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wohlfahrt et al. and Kenan et al. as applied to claims 1, 3-5 and 19-24 above, and further in view of Byalina et al.

Wohlfahrt et al. and Kenan et al. in combination teach a method of generating libraries mutants galactose oxidase genes and screening for mutants that are resistant to oxidation by peroxidases.

The difference between the teachings of the two references and the claimed invention is that the two references do not teach a method of utilizing fluorescence techniques in screening for active glucose oxidases.

However, fluorescence techniques in screening for active proteins are well known and practiced in the art. For example, Bylina et al. teach a method of screening colonies and determining kinetics and spectral data (Columns 2 through 4). The method of Bylina et al. employs fluorescence in its assays and various colored products (Columns 8-12). In the state of the art, there are many known colored products that can be used, including Leo Crystal Violet available through Aldrich (Aldrich Catalog 1998-1999).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to use fluorescence technique to screen for active galactose oxidases. The motivation of screening colonies having active

galactose oxidase is to efficiently screen for the mutant enzymes instead of isolating and purifying enzymes. One of ordinary skill in the art would have had a reasonable expectation of success since site-directed and random mutagenesis is routinely performed in the art and Bylina et al. teach successful screening assays of colonies containing mutant proteins.

Claims 10-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wohlfahrt et al. and Kenan et al. as applied to claims 1, 3-5 and 19-24 above, and further in view of Shtelzer.

Wohlfahrt et al. and Kenan et al. in combination teach a method of generating libraries mutants galactose oxidase genes and screening for mutants that are resistant to oxidation by peroxidases.

The difference between the teachings of the two references and the claimed invention is that the two references do not teach a method of utilizing biosensors for screening for active galactose oxidases.

However, use of biosensors to detect samples containing galactose oxidases is well known and practiced in the art. Shtelzer et al. (form PTO-892) teach a biosensor comprising an glucose oxidase (abstract).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to a biosensor to screen for active galactose oxidases. The motivation of screening colonies having active galactose oxidase is to efficiently screen for the mutant enzymes instead of isolating and purifying enzymes.

One of ordinary skill in the art would have had a reasonable expectation of success since site-directed and random mutagenesis is routinely performed in the art and Shtelzer et al. teach successful screening assays of colonies containing mutant proteins.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 703-308-9363. The examiner can normally be reached on 6:30 A.M. to 5:00 P.M. Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 703-308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Yong D. Pak
Patent Examiner

December 15, 2003

PONNATHAPU ACHUTAMURTHY
SUPERVISORY PATENT EXAMINER
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